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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,905	11/10/2000	Kalyanaraman Ramnarayan	24737-1906C	3606

7590

12/03/2002

HELLER, EHRMAN, WHITE & MCAULIFFE, LLP
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EXAMINER

BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 12/03/2002

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/709,905

Applicant(s)

RAMNARAYAN ET AL.

Examiner

John S. Brusca

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 September 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25,45-50,66,67 and 87-90 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25,45-50,66,67 and 87-90 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3, 12, 16, 17, 19, 21, 25
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1 in Paper No. 24 is acknowledged.

The applicants point to two errors in the restriction requirement mailed 07 August 2002.

The applicants state that claims 84-86 should have been listed in Group 2 and were incorrectly listed in Group 6. Upon review it is agreed that the applicants are correct and the restriction requirement is hereby corrected to list claims 84-86 in Group 2 rather than in Group 6. The applicants further state that claim 28 was not listed in any group. Upon review it is agreed that claim 28 is part of Group 1. It is further noted that claim 28 has been cancelled in the amendment filed 06 September 2002. Should applicants file an amendment in the future which adds a new claim drawn to the subject matter of cancelled claim 28, the claim would be examined as part of the elected invention.

Drawings

New corrected drawings are required in this application because as noted on the attached Form PTO 948, figure 11 should be renumbered so that each sheet has a numeral in the name of the figure. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

It is further noted that the request to amend the drawings in the amendment filed 26 March 2001 was not entered because the Office does not amend drawings. The attached Form PTO 948 refers to the formal drawings filed on 17 October 2002.

Inventorship

In view of the papers filed 06 September 2002, the inventorship in this nonprovisional application has been changed by the deletion of P Patrick Hess.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Information Disclosure Statement

Some items in the Information Disclosure Statements of papers 3, 16, and 17 are indicated as not considered because a copy of the references was not provided, or because a translation or statement of relevance was not provided.

A fee for the Information Disclosure Statement filed 08 October 2002 was charged in error. The fees should be refunded at the time of mailing of this Office action. The applicants may wish to verify refunding of this fee.

Specification

The sequence listing and computer readable form filed 04 September 2001 has been entered into the specification and STIC database.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25, 45-50, 66, 67, and 87-90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must generate three dimensional protein structural variant models from amino acid sequence data. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The specification does not present specific guidance to determine the structure of a polypeptide from sequence data.

c) The specification does not present a working model of determination of the structure of a polypeptide from sequence data.

d) The nature of the invention, designing drugs that interact with a three dimensional structure of a protein that is determined solely from use of sequence data, is complex.

e) Sternberg et al. (reference A on the Form PTO 1449 filed 08 October 2002) and Koehl et al. (reference B on the Form PTO 1449 filed 08 October 2002) review a meeting held in late 1998 known as CASP3. CASP3 was designed to test contemporary polypeptide structure

prediction methods in a blind contest. Various classes of structure determination methods were used to predict structures that were recently experimentally determined but whose structure was not available to the participants of CASP3 until after submission of their structure predictions. Thus, the accuracy of the predictions could be predicted by comparison to the corresponding polypeptide structures. Koehl et al. and Sternberg et al. show that there were three types of algorithms employed. The first were used on sequences that had a significant degree of similarity to known polypeptide structures (comparative modeling). The second type of algorithm was used on sequences with folding domains with a significant degree of similarity to known polypeptide domains (fold recognition). The third type of algorithm relied either partially or not at all on structural predictions based on similarity to known polypeptides (ab initio prediction). Both figure 2 of Sternberg et al. and table 1 of Koehl et al. show that for sequences with "new folds", i.e., sequences without significant similarity to known polypeptide structures, the ab initio algorithms had a relatively poor ability to predict structure, and predicted the positions of only about half of the residues of the sequence. Sternberg et al. and Koehl et al. demonstrate that at the effective filing date of the instant application, knowledge of known polypeptide structures with similarity to a polypeptide sequence of interest was of great benefit in predicting the structure of the polypeptide sequence of interest. Sternberg et al. and Koehl et al. further show that at the effective filing date of the instant application, the best ab initio methods were unable to accurately predict structures of complete polypeptides in the absence of knowledge of structures of polypeptides with similarity to the polypeptide sequence of interest. It is apparent that the claimed method requires an ab initio method to accurately predict the structure of a polymorphic polypeptide sequence in the absence of additional structural information.

f) The skill of those in the art of polypeptide structure and modeling is high.

g) Both Sternberg et al. and Koehl et al. show that ab initio methods of structure prediction from polypeptide sequence information alone is not predicted to result in an accurate structure of a complete polypeptide.

h) The claims are broad in that they are drawn to modeling polypeptide structures in the absence of information other than sequence information.

The skilled practitioner would first turn to the instant application for guidance in practicing the claimed method. However, the instant application does not provide specific guidance to predict structures of polypeptides in the absence of information other than sequence information. The skilled practitioner would next turn to the prior art, but the prior art does not provide adequate guidance to practice the claimed invention as discussed above. Finally, said practitioner would turn to trial and error experimentation to practice the claimed invention. Such represents undue experimentation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00.

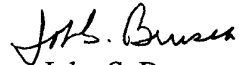
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4025. The fax phone numbers for the organization where this application or proceeding is assigned are 703 746-5137 for regular communications and 703 746-5137 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.



John S. Brusca
Primary Examiner
Art Unit 1631

jsb
November 27, 2002